

## PATENT COOPERATION TREATY

## PCT

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	<b>FOR FURTHER ACTION</b> see Form PCT/ISA/220 as well as, where applicable, item 5 below.	
International application No.  PCT/IB2004/004335	International filing date: (day/month/year)  06/12/2004	(Earliest) Priority Date (day/month/year)  05/12/2003
Applicant  UNIVERSITY OF GRONINGEN		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 5 sheets.



It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.



The international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. ☒ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.

2. ☐ **Certain claims were found unsearchable** (See Box II).

3. ☐ **Unity of invention is lacking** (see Box III).

4. With regard to the **title**,



the text is approved as submitted by the applicant.



the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,



the text is approved as submitted by the applicant.



the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. With regard to the **drawings**,

- a. the figure of the **drawings** to be published with the abstract is Figure No. 20



as suggested by the applicant.



as selected by this Authority, because the applicant failed to suggest a figure.



as selected by this Authority, because this figure better characterizes the invention.

- b. ☐ none of the figures is to be published with the abstract.

# INTERNATIONAL SEARCH REPORT

International application No.

PCT/IB2004/004335

## Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.b of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, the international search was carried out on the basis of:
  - a. type of material
    - ☒ a sequence listing
    - ☒ table(s) related to the sequence listing
  - b. format of material
    - ☒ in written format
    - ☒ in computer readable form
  - c. time of filing/furnishing
    - ☐ contained in the international application as filed
    - ☐ filed together with the international application in computer readable form
    - ☒ furnished subsequently to this Authority for the purpose of search
2. ☒ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
3. Additional comments:

A. CLASSIFICATION OF SUBJECT MATTER  
IPC 7 C07K14/705 G06F19/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)  
IPC 7 C07K G06F

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, Sequence Search, CHEM ABS Data, BIOSIS, EMBASE, WPI Data, PAJ

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 03/029420 A (GENENTECH, INC; KELLEY, ROBERT F; LINDSTROM, STEPHANIE H) ✓ 10 April 2003 (2003-04-10) claim 1 & DATABASE Geneseq 'Online! 4 December 2003 (2003-12-04), "Human Apo-2 ligand protein mutant D234C." retrieved from EBI accession no. GSP:ADB61491 Database accession no. ADB61491	1-62
X	WO 99/36535 A (GENENTECH, INC; ASHKENAZI, AVI, J; KELLEY, ROBERT, F; O'CONNEL, MARK,) 22 July 1999 (1999-07-22) examples 18,19 ----- -/--	1-62

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

\* Special categories of cited documents :

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

- \*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- \*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- \* & \* document member of the same patent family

Date of the actual completion of the international search

14 April 2005

Date of mailing of the international search report

02/05/2005

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax (+31-70) 340-3016

Authorized officer

Petri, B

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>WO 01/00832 A (GENENTECH, INC)  ✓ 4 January 2001 (2001-01-04)  table 1</p> <p>-----</p>	1-62
X	<p>WO 88/06625 A (CETUS CORPORATION)  7 September 1988 (1988-09-07)  abstract</p> <p>-----</p>	1-62
P,X	<p>WO 2004/001009 A (GENENTECH, INC;  ✓ HYMOWITZ, SARAH; KELLEY, ROBERT, F;  LINDSTROM, STEPHAN)  31 December 2003 (2003-12-31)  cited in the application  the whole document</p> <p>-----</p>	1-62
P,X	<p>VAN DER SLOOT ALMER M ET AL:  "Stabilization of TRAIL, an all-beta-sheet  multimeric protein, using computational  redesign."  PROTEIN ENGINEERING, DESIGN &amp; SELECTION :  PEDS. SEP 2004,  vol. 17, no. 9, September 2004 (2004-09),  pages 673-680, XP002324633  ISSN: 1741-0126  the whole document</p> <p>-----</p>	1-62

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 03029420	A	10-04-2003	CA 2461292 A1 EP 1501866 A2 WO 03029420 A2 US 2004186051 A1	10-04-2003 02-02-2005 10-04-2003 23-09-2004
WO 9936535	A	22-07-1999	AU 2325199 A CA 2318029 A1 EP 1045906 A1 JP 2002508962 T WO 9936535 A1 US 6740739 B1	02-08-1999 22-07-1999 25-10-2000 26-03-2002 22-07-1999 25-05-2004
WO 0100832	A	04-01-2001	AU 6338200 A CA 2377585 A1 CN 1370232 A EP 1194555 A1 JP 2003503057 T MX PA01013236 A NZ 515990 A WO 0100832 A1	31-01-2001 04-01-2001 18-09-2002 10-04-2002 28-01-2003 21-06-2002 31-10-2003 04-01-2001
WO 8806625	A	07-09-1988	AU 1346488 A WO 8806625 A2	26-09-1988 07-09-1988
WO 2004001009	A	31-12-2003	AU 2003247609 A1 WO 2004001009 A2	06-01-2004 31-12-2003

## INTERNATIONAL SEARCH REPORT

PCT/IB2004/004335

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07K14/705 G06F19/00

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07K G06F

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, Sequence Search, CHEM ABS Data, BIOSIS, EMBASE, WPI Data, PAJ

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 03/029420 A (GENENTECH, INC; KELLEY, ROBERT F; LINDSTROM, STEPHANIE H) 10 April 2003 (2003-04-10) claim 1 & DATABASE Geneseq 'Online! 4 December 2003 (2003-12-04), "Human Apo-2 ligand protein mutant D234C." retrieved from EBI accession no. GSP:ADB61491 Database accession no. ADB61491	1-62
X	WO 99/36535 A (GENENTECH, INC; ASHKENAZI, AVI, J; KELLEY, ROBERT, F; O'CONNEL, MARK,) 22 July 1999 (1999-07-22) examples 18,19 ----- -/--	1-62

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

## \* Special categories of cited documents:

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

- \*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- \*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
- \*G\* document member of the same patent family

Date of the actual completion of the international search

14 April 2005

Date of mailing of the international search report

02/05/2005

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax (+31-70) 340-3016

Authorized officer

Petri, B

## INTERNATIONAL SEARCH REPORT

PCT/IB2004/004335

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 01/00832 A (GENENTECH, INC) 4 January 2001 (2001-01-04) table 1 -----	1-62
X	WO 88/06625 A (CETUS CORPORATION) 7 September 1988 (1988-09-07) abstract -----	1-62
P,X	WO 2004/001009 A (GENENTECH, INC; HYMOWITZ, SARAH; KELLEY, ROBERT, F; LINDSTROM, STEPHAN) 31 December 2003 (2003-12-31) cited in the application the whole document -----	1-62
P,X	VAN DER SLOOT ALMER M ET AL: "Stabilization of TRAIL, an all-beta-sheet multimeric protein, using computational redesign." PROTEIN ENGINEERING, DESIGN & SELECTION : PEDS. SEP 2004, vol. 17, no. 9, September 2004 (2004-09), pages 673-680, XP002324633 ISSN: 1741-0126 the whole document -----	1-62

## INTERNATIONAL SEARCH REPORT

PCT/IB2004/004335

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 03029420	A	10-04-2003	CA 2461292 A1	10-04-2003
			EP 1501866 A2	02-02-2005
			WO 03029420 A2	10-04-2003
			US 2004186051 A1	23-09-2004
WO 9936535	A	22-07-1999	AU 2325199 A	02-08-1999
			CA 2318029 A1	22-07-1999
			EP 1045906 A1	25-10-2000
			JP 2002508962 T	26-03-2002
			WO 9936535 A1	22-07-1999
			US 6740739 B1	25-05-2004
WO 0100832	A	04-01-2001	AU 6338200 A	31-01-2001
			CA 2377585 A1	04-01-2001
			CN 1370232 A	18-09-2002
			EP 1194555 A1	10-04-2002
			JP 2003503057 T	28-01-2003
			MX PA01013236 A	21-06-2002
			NZ 515990 A	31-10-2003
			WO 0100832 A1	04-01-2001
WO 8806625	A	07-09-1988	AU 1346488 A	26-09-1988
			WO 8806625 A2	07-09-1988
WO 2004001009	A	31-12-2003	AU 2003247609 A1	06-01-2004
			WO 2004001009 A2	31-12-2003